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PATENT
Attorney Docket No. DOW-04647

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	George Peter Lomonossoff *et al.*		
Serial No.:	09/580,704	Group No.:	1636
Filed:	05/30/00	Examiner:	Sandals, W.
Entitled:	**Modified Plant Viruses As Vectors**		

INFORMATION DISCLOSURE STATEMENT TRANSMITTAL

Assistant Commissioner for Patents
Washington, D.C. 20231

CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.8(a)(1)(i)(A)

I hereby certify that this correspondence (along with any referred to as being attached or enclosed) is, on the date shown below, being deposited with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.

Dated: August 19, 2002 By: _____
Christopher J. Collins

Sir or Madam:

Enclosed please find an Information Disclosure Statement and Form PTO-1449, including copies of the references contained thereon, for filing in the U.S. Patent and Trademark Office.

A check for $180.00 is also enclosed pursuant to 37 C.F.R. § 1.17(p) for filing this Information Disclosure Statement after three months as set forth in 37 C.F.R. § 1.97(c).

The Commissioner is hereby authorized to charge any additional fee or credit overpayment to our Deposit Account No. **08-1290**. **An originally executed duplicate of this transmittal is enclosed for this purpose.**

Dated: August 19, 2002

_____
David J. Wilson
Registration No. 45,225

MEDLEN & CARROLL, LLP
101 Howard Street, Suite 350
San Francisco, California 94105
415/904-6500

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Sir or Madam:

The citations listed below, copies attached, may be material to the examination of the above-identified application, and are therefore submitted in compliance with the duty of disclosure defined in 37 C.F.R. §§ 1.56 and 1.97. The Examiner is requested to make these citations of official record in this application.

The following printed publications are referred to in the body of the specification:

- Ahlquist, P., and Janda, M., "cDNA Cloning and In Vitro Transcription of the Complete Brome Mosaic Virus Genome," *Mol. Cell Biol.* 4:2876-2882 (1984);
- Biggin, M.D. *et al.*, "Buffer gradient gels and ^{35}S label as an aid to rapid DNA sequence determination," *Proc. Natl. Acad. Sci. USA* 80:3963-3965 (1983);
- Blirnboim, H.C. and Doly, J.,"A rapid alkaline extraction procedure for screening recombinant plasmid DNA," *Nucleic Acids Res.* 7:1513-1523 (1979);
- Chanh, T.C., *et al.*, "Induction of anti-HIV neutralizing antibodies by synthetic peptides," *EMBO J.* 5:3065-3071 (1986);

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- Dalgleish, A.G., *et al.*, "Neutralization of Diverse HIV-1 Strains by Monoclonal Antibodies Raised against a gp41 Synthetic Peptide," *Virology* 165:209-215 (1988);
- De Varennes, A. and Maule, A.J., "Independent Replication of Cowpea Mosaic Virus Bottom Component RNA:*In Vivo* Instability of the Viral RNAs," *Virology* 144:495-501 (1985);
- Dessens, J.T. and Lomonossoff, G.P., "Mutational Analysis of the Putative Catalytic Triad of the Cowpea Mosaic Virus 24K Protease," *Virology* 184:738-746 (1991);
- Feinberg, A.P. and Vogelstein, B., "A Technique for Radiolabeling DNA Restriction Endonuclease Fragments to High Specific Activity," *Analytical Biochem.* 132:6-13 (1983);
- Goldbach, R., *et al.*, "Independent replication and expression of B-component RNA of cowpea mosaic virus," *Nature* 286:297-300 (1980;
- Holness, C.L. (1989). PhD Thesis, University of Warwick;[1]
- Holness, C.L., *et al.*, "Identifcation of the Initiation Codons for Translation of Cowpea Mosaic Virus Middle Component RNA Using Site-Directed Mutagenesis of an Infectious cDNA Clone," *Virology* 272:311-320 (1989);
- Kennedy, R.C., *et al.*, "Antiserum to a Synthetic Peptide Recognizes the HTLV-III Envelope Glycoprotein," *Science* 231:1556-1559 (1986);
- Kunkel, T.A., "Rapid and efficient site-specific mutagenesis without phenotypic selection," *Proc. Nat. Acad. Sci. USA* 82:488-492 (1985);
- Laemmli, U.K., "Cleavage of Structural Proteins during the Assembly of the Head of Bacteriophage T4," *Nature* 227:680-685 (1970);
- Lehrach, H., *et al.*, "RNA Molecular Weight Determinations by Gel Electophoresis under Denaturing Conditions, a Critical Reexamnation," *Biochemistry* 16:4743-4751 (1977);
- Lomonossoff, G.P.,*et al.*, "The location of the first AUG codons in cowpea mosaic virus RNAs," *Nucleic Acids Research* 10:4861-4872 (1982);

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[1] We have been unable to locate this reference. If the examiner so requests, we can increase our efforts to obtain a copy.

- Lomonossoff, G.P. and Shanks, M., "The nucleotide sequence of cowpea mosaic virus B RNA," *EMBO J.* 2: 2253-2258 (1983);
- Maniatis, T., Fritsch, E.F. and Sambrooke, J. (1982). Molecular Cloning. A Laboratory Manual. Cold Spring Harbor Laboratory;[2]
- Pelham, H.R.B. and Jackson, R.J., "An Efficient mRNA-Dependent Translation System from Reticulocyte Lysates," *Eur. J. Biochem.* 67:247-256 (1976);
- Sanger, F., et al., "Cloning in Single-stranded Bacteriophage as an Aid to Rapid *J. Mol. Biol.* 143:161-178 (1980);
- Shanks, M., et al., "The Primary Structure of Red Clover Mottle Virus Middle Component RNA," *Virology* 155:697-706 (1986);
- van Wezenbeek, *et al.*, "Primary structure and gene organization of the middle-component RNA of cowpea mosaic virus," *EMBO J.* 2:941-946 (1983); and
- Ziegler-Graff, *et al.*, "Biologically Active Transcripts of Beet Necrotic Yellow Vein Virus RNA-3 and RNA-4," *J. Gen. Virol.* 69:2347-2357 (1988).

Applicants have become aware of the following printed publications which may be material to the examination of this application:

- WO patent 89/08145 to Grill *et al.* discloses viral vectors comprising heterologous sequences which can be used to infect cells which will then produce a product. Prokaryotic and eukaryotic, including plant and animal, viral vectors are disclosed. Unlike the present invention, there is no disclosure of foreign sequences inserted within the coat protein coding region such that the modified coat proteins are expressed in a host or host tissue and are capable of assembly into viral particles.
- WO patent 90/00611 to Erwin and Grill discloses viral vectors which can be used to infect cells which will then produce an enzyme which can be used to purify a stereoisomer from a racemic mixture. The viral vectors are biologically contained, due to deletion, mutation or other alteration of the viral coat protein gene, such that no biologically functional coat protein can be expressed.

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[2] This reference was cited in the application as filed, for general reference without any specific page numbers, therefore a hard copy of the reference is not included.

Although there is disclosure of fusion proteins resulting from insertion of a nucleotide sequence into or adjacent to a capsid protein sequence of a viral nucleic acid, there is no disclosure of the resulting fusion proteins being capable of assembling a viral capsid when expressed in an appropriate host or host tissue.

- WO patent 87/06261 to Wilson discloses a packaging system for chimeric RNA molecules. Expression of the encapsidated chimaeric RNAs was observed in plants (tobacco mesophyll protoplasts and pea leaf epidermis following infection of a leaf) and animals (*Xenopus* oocytes). Unlike the present invention, there is no discussion of insertion of foreign sequences into viral coat protein coding regions and subsequent assembly of modified coat proteins into an intact virus.
- European Patent 0 278 667 B1 to Ahlquist *et al.* discloses hybrid RNA viruses. These viruses have sequences from an infectious virus fused to the origin of assembly sequence and coat protein sequence of a rod shaped virus. The sequence of the infectious virus is altered to inactivate its own coat protein genes, and may also include heterologous nucleic acid sequences to direct expression of genes of interest in an infected host, including plants. There is no disclosure of insertion of foreign sequences into the coat protein coding region of a virus such that the expression of the modified coat proteins is permissive for viral assembly.
- European Patent 0 194 809 A1 to Ahlquist and French discloses RNA vectors suitable for transformation of appropriate hosts. It is disclosed that the coat protein coding regions of the RNA virus may be altered by insertion of, or replacement by the exogenous sequence of interest, at least in viruses for which the coat proteins are not essential for replication. It is stated that any insertions of exogenous sequences must be in regions which are nonessential for viral replication within the host. Although an in-frame fusion between the first seven nucleotides of the BMV coat protein gene and the bacterial chloramphenicol acetyltransferase coding sequence and an insertion of the bacterial chloramphenicol acetyltransferase coding sequence into the BMV coat protein

coding sequence are disclosed, there is no discussion of the ability of such fusion proteins to be competent for viral assembly, a requirement of the present invention.

- U.S. Patent 4,407,956 to Howell discloses a plant vector based on cauliflower mosaic virus, a representative DNA plant virus. The viral DNA is cloned into a suitable cloning vector, and can then be manipulated after propagation of the cloned vector. The genetic manipulation includes introduction of an oligonucleotide linker or other heterologous sequences into the viral DNA sequence. The importance of not disrupting regions of the virus essential to replication and spread during a systemic plant infection is emphasized. An example of an insertion into an intergenic region is provided. There is no disclosure of insertion of a foreign sequence specifically into a coat protein region which will permit viral assembly in a plant or plant material.
- U.S. Patent 4,593,002 to Dulbecco describes the production of viruses which carry foreign protein segments on exposed portions of their surface proteins. These viruses can be used as potential vaccines to raise immune responses against the surface-expressed foreign protein segments. This patent is silent on the use of plant viruses.
- U.S. Patent 4,956,282 to Goodman et al. discloses a method of expressing physiologically active mammalian and mammalian viral pathogen proteins, including viral surface antigens, in plant cells. There is no disclosure of plants infected with a virus which has a foreign sequence inserted into a coat protein coding sequence.
- U.S. Patent 4,722,840 to Valenzuela *et al.*, describe viral particles having hybrid particle-forming proteins. These hybrid proteins are expressed on the surface of the particle, and still permit particle formation. The hybrid proteins are formed by an end-to-end fusion of the particle forming protein and the protein or epitope of interest, resulting in an alteration of the terminus of the particle forming protein. When expressed in the host, the hybrid proteins assemble into capsids. There is no discussion of plants or plant viruses.

- European Patent 0 221 044 B1 to Rogers, *et al.* discloses the utilization of a portion of the TGMV (geminivirus) coat protein to facilitate the self-replication of desired sequences in plant cells. Whole virus is not produced. This publication does not teach the insertion of a nucleic acid (plant or non-plant) coding for a foreign peptide wherein the insertion of the foreign nucleic acid is inserted such that there is no significant interference with the capacity of the modified virus to assemble.
- European Patent 0 174 759 A1 to James, *et al.* discloses the synthesis of a plasmid containing the TMV coat protein and a hapten (antigenic isotope) that can be expressed in a bacteria (*e.g.*, *E. coli*) wherein the coat protein/hapten is translated and self assembles. Whole virus is not produced. This publication does not teach the insertion of a nucleic acid coding for a foreign peptide into the genomic nucleic acid of a virus wherein the insertion of the foreign nucleic acid does not significantly interfere with the capacity of the modified virus to assemble.
- Abad-Zapatero, C. *et al.*, "Structure of southern bean mosaic virus at 2.8 Å resolution," *Nature* 286:33-39 (1980) describe X-ray diffraction studies of native and heavy atom derivatized crystals of the southern bean mosaic virus. A b-barrel structure was found to be the dominant structural feature. The structure of southern bean mosaic virus was found to closely resemble that of tomato bushy stunt virus, and the evolutionary implications of this similarity are discussed. There is no discussion of a genetically modified plant virus with a foreign peptide-encoding sequence inserted into the genome.
- Abstract W47-007 - Submitted to 8th International Congress to Virology in Berlin (1990). This abstract outlines an investigation of structure-properties relationships in the cowpea mosaic virus by mutational analysis of the coat protein coding region of the M (middle) RNA. Experiments addressing the possibility of expressing heterologous protein sequences on the capsid surface are mentioned, however, experimental details and results are not provided in the abstract. The generation of a plant infected with a modified virus is not disclosed.

- Argos *et al.*, "Similarity in gene organization and homology between proteins of animal picornaviruses and a plant comovirus suggest common ancestry of these virus families," *Nucleic Acids Research* 12(18):7251-7267 (1984) describe a comparison of the deduced amino acid sequence of several animal picornaviruses with one another and with cowpea mosaic virus, a plant comovirus. Homologies between the animal and plant viruses were found in several regions. There is no discussion of a plant infected with a modified virus, or of modified plant viral particles.
- Chen *et al.*, "Capsid Structure and RNA Packaging in Comoviruses," Seminars in Virology 1:453-466 (1990) provide a review of comovirus capsid structure and RNA packaging. Cowpea mosaic virus and bean pod mottle virus are used as the primary examples. There is discussion of the use of infectious clones to propagate site-directed mutations in the capsid proteins, which can then be used to probe capsid structure. There is also non-enabling discussion of inserting foot and mouth disease virus antigen into an exposed loop of the cowpea mosaic virus structure, and attempts to propagate this chimera in plants. However, there is no discussion of whether such insertions will be permissive for viral assembly, which is a requirement of the present invention.
- Chen *et al.*, "Protein-RNA Interactions in an Icosahedral Virus at 3.0 Å Resolution," *Science* 245:154-159 (1989) describe the structure of RNA2-containing bean-pod mottle virus capsids as well as the sequence of the coat protein, derived from viral cDNAs. There is no discussion of plants infected with a modified virus or of plant virus particles comprising coat proteins with an insertion of a foreign peptide.
- Crabbe *et al.*, "Modelling of poliovirus HIV-1 antigen chimaeras," *FEBS Letters* 271:194-198 (1990) describe a method to model chimeric viral constructs, and correlate predicted parameters with viral viability. There is no discussion of plants infected with a modified virus, or of modified plant viral particles.
- Evans *et al.*, "An engineered poliovirus chimaera elicits broadly reactive HIV-1 neutralizing antibodies," *Nature* 339:385-388 (1989) describe the development

of a chimeric, attenuated poliovirus containing an HIV-1 gp41 epitope inserted into the VP1 capsid protein sequence. There is no discussion of plants infected with modified viruses or of modified plant virus particles.

- Fox , "No winners against AIDS," *Bio/Technology* 12:128 (1994) provides a summary of research presented at the "First National Conferences on Human Retroviruses and Related Infections". The highlighted research includes the role of cytotoxic T lymphocytes, vaccine development strategies and cytokine therapy. There is no discussion of plants infected with a modified virus or of modified plant virus particles.
- Gorbalenya *et al.*, "An NTP-Binding Motif is the Most Conserved Sequence in a Highly Diverged Monophyletic Group of Proteins Involved in Positive Strand RNA Viral Replication," *J. of Mol Evol* 28:256-268 (1989) describe a phylogenetic analysis of positive sense, single-stranded RNA viruses, including plant comoviruses, based on an NTP motif found in nonstructural proteins. The analysis distinguished three distinct families of NTP motif-containing proteins. There is no discussion of plants infected with a modified virus or of modified plant viruses assembled from insertionally-modified coat proteins.
- Harrison. S.C. *et al.*, "Tomato bushy stunt virus at 2.9 Å resolution," *Nature* 276:368-373 (1978) describe X-ray diffraction studies on crystallized native and heavy atom derivatized tomato bushy stunt virus. There is no discussion of plants infected with modified viruses or of modified viral particles assembled from coat proteins containing a foreign peptide.
- Hayes, R.J., *et al.*, "Stability and expression of bacterial genes in replicating geminivirus vectors in plants," *Nucleic Acids Research* 17(7):2391-2403 (1989) describe tomato golden mosaic virus vector constructs, in which the coat protein gene (or most of the gene) is replaced by bacterial *gus* or *neo* genes. Unlike the present invention, there is no discussion of viral assembly as a result of coat protein replacement/deletion constructs, and no discussion of expression of the coat protein containing an insertion of a foreign nucleotide sequence.
- Haynes *et al.*, "Development of a Genetically-Engineered, Candidate Polio Vaccine Employing the Self-Assembling Properties of the Tobacco Mosaic

Virus Coat Protein," *Bio/Technology* 4:637-641 (1986) describe a genetically engineered vaccine system. Tobacco mosaic virus coat protein constructs with a C-terminal insertion of a poliovirus epitope were expressed in *E. coli*, then allowed to self-assemble in vitro, either by lowering the pH to 5.0 or by inclusion of TMV genomic RNA. The assembled particles induced poliovirus neutralizing antibodies following injection into rats. There is no discussion of plants infected with a modified virus or of expression and assembly of modified viral particles in plants or plant material.

- Hogle, J.M. *et al.*, "Structure and Assembly of Turnip Crinkle Virus I. X-ray Crystallographic Structure Analysis at 3.2 Å Resolution," *J. Mol. Biol.* 191:625-638 (1986) describe X-ray diffraction studies on crystallized methyl mercury adducts of turnip crinkle virus. There is no discussion of plants infected with a genetically modified virus or of modified viral particles comprising a coat protein with an inserted foreign peptide sequence.
- Liljas, L. *et al.*, "Structure of Satellite Tobacco Necrosis Virus at 3.0 Å Resolution," *J. Mol. Biol.* 159:93-108 (1982) describe X-ray diffraction studies to elucidate the structure of heavy atom derivatived satellite tobacco necrosis virus crystals. There is no discussion of plants infected with a genetically modified virus or of modified plant virus particles comprising a coat protein with an inserted foreign peptide.
- Lomonossoff *et al.*, "The Synthesis and Structure of Comovirus Capsids," *Prog Biophys Mol Biol.* 55:107-137 (1991) review comovirus capsid structure, synthesis and assembly. Although several mutational analyses are briefly discussed, and the benefit of future mutational analyses to examine the role of specific amino acids in viral structure and assembly is suggested, none specifically disclose the insertion of a foreign nucleotide sequence into the coat protein coding region and subsequent viral infection and assembly in a plant.
- Namba, N., *et al.*, "Structure of Tobacco Mosaic Virus at 3.6 Å Resolution: Implications for Assembly," *Science* 231:1401-1406 (1986) describe X-ray fiber diffraction analysis of the tobacco mosaic virus structure in native and heavy atom derivatives. There is no discussion of plants infected with a genetically

modified virus, or of modified plant virus particles comprising a coat protein with an inserted foreign peptide.

- Rose, C.S. and D. J. Evans, "Poliovirus antigen chimeras," *TIBTECH* 9:415-412 (1991) review work on construction of polioviruses that can be used as "epitope presentation systems". These chimeric viruses express foreign epitopes at the poliovirus antigenic site 1. Foreign epitopes have been expressed from a variety of viruses, including HPV-16, HIV-1, hepatitis A and FMDV. Applications of the chimeras in vaccines, serodiagnosis and monoclonal antibody production are discussed. The importance of retention of virus viability, including assembly of processed capsid precursors, is noted. There is no discussion of plants infected with a modified virus or of a modified plant virus particle comprising coat proteins with inserted foreign peptides.
- Rossmann *et al.*, "Icosahedral RNA Virus Structure, in *Annual Reviews of Biochemistry* 58:533-573 (1989) review the structure of icosahedral RNA virus structure. There is no discussion of plants infected with a genetically modified virus, or of a modified plant virus comprising coat proteins with inserted foreign peptides.
- Stauffacher, C.V. *et al.*, "The Structure of Cowpea Mosaic Virus at 3.5 Å Resolution," Crystallography in Molecular Biol. pp. 293-308 (1985) discloses the X-ray crystallography structure of the Cowpea Mosaic virus at 3.5 Å resolution. There is no discussion of plants infected with a genetically modified virus, or of a modified plant virus comprising coat proteins with inserted foreign peptides.
- Takamatsu, N., *et al.*, "Production of enkephalin in tobacco protoplasts using tobacco mosaic virus RNA vector," *FEBS Letters* 269 (1):73-76 (1990) describe tobacco mosaic virus RNA vector constructs designed to produce functional fusion proteins between the tobacco mosaic virus coat protein C-terminus and other proteins. Infection of plants with a coat protein reconstituted transcript containing an insertion of a foreign enkephalin sequence did not appear to result in viral particle assembly, while infection of plants with a coat protein reconstituted transcript containing a mutation which extended the peptide

sequence of the coat protein at the C terminus was capable of forming virus particles. Both transcripts were capable of directing fusion protein expression following electroporation into protoplasts. This reference did not disclose the construction of a viral RNA vector wherein the exogenous sequence was inserted into the viral coat protein sequence and such insertion did not inhibit viral assembly.

- Wimmer, "Genome-Linked Proteins of Viruses," *Cell* 28:199-201 (1982) reviews the literature pertaining to VPgs, which are proteins covalently bonded to the genomes of some ssRNA and dsDNA viruses, including the plant comoviruses. Polioviruses are discussed as examples of RNA viruses, and adenoviruses provide the example for dsDNA viruses. There is no discussion of plants infected with a modified virus, or of modified viral particles comprising a coat protein with an inserted foreign sequence.
- Ahlquist *et al.*, "Molecular Studies of Brome Mosaic Virus Using Infectious Transcripts from Cloned cDNA" Adv. Virus. Res. 32:215-42 (1987) describe a modified Brome Mosaic Virus in which the coat protein has been replaced with a CAT gene or fused to a CAT gene. Ahlquist *et al.* do not disclose a modified virus comprising a coat protein containing an foreign peptide insert, wherein the coat proteins are able to assemble to form a modified virus.
- French *et al.*, "Bacterial Gene Inserted in an Engineered Plant Virus: Efficient Expression in a Monocotyledenous Plant" Science 231:1294-97 (1986) describe a modified Brome Mosaic Virus in which the coat protein has been replaced with a CAT gene or fused to a CAT gene. French *et al.* do not disclose a modified virus comprising a coat protein containing an foreign peptide insert, wherein the coat proteins are able to assemble to form a modified virus.
- Janda *et al.*, High Efficiency T7 Polymerase Synthesis of Infectious RNA from Cloned Brome Mosaic Virus cDNA and Effect of 5' Extensions on Transcript Infectivity" disclose that addition of 5' non-viral sequences to viral RNAs reduces infectivity. Janda *et al.* do not disclose a modified virus comprising a coat protein containing an foreign peptide insert, wherein the coat proteins are able to assemble to form a modified virus.

- Eggen *et al.* "Improvements of the Infectivity of In Vitro Transcripts from Cloned Cowpea Mosaic Virus cDNA: Impact of terminal Nucleotide Sequences" Virology 173:447-55 (1989) disclose that addition of 5' non-viral sequences to viral RNAs reduces infectivity. Eggen *et al.* do not disclose a modified virus comprising a coat protein containing an foreign peptide insert, wherein the coat proteins are able to assemble to form a modified virus.
- Eggen *et al.*, "Analysis of Sequences Involved in Cowpea Mosaic Virus RNA Replication Using Site Specific Mutants" Virology 173:456-64 (1989) disclose the function of 3' sequences of cowpea mosaic virus. Eggen *et al.* do not disclose a modified virus comprising a coat protein containing an foreign peptide insert, wherein the coat proteins are able to assemble to form a modified virus.
- Ahlquist *et al.*, U.S. Pat. Nos. 5,500,360 disclose a modified Brome Mosaic Virus in which the coat protein has been replaced with a CAT gene or fused to a CAT gene. Ahlquist *et al.* do not disclose a modified virus comprising a coat protein containing an foreign peptide insert, wherein the coat proteins are able to assemble to form a modified virus.
- Ahlquist *et al.*, U.S. Pat. Nos. 5,846,795 disclose a modified Brome Mosaic Virus in which the coat protein has been replaced with a CAT gene or fused to a CAT gene. Ahlquist *et al.* do not disclose a modified virus comprising a coat protein containing an foreign peptide insert, wherein the coat proteins are able to assemble to form a modified virus.
- Ahlquist, U.S. Pat. 4,885,248, discloses a modified Brome Mosaic Virus in which the coat protein has been replaced with a CAT gene or fused to a CAT gene. Ahlquist does not disclose a modified virus comprising a coat protein containing an foreign peptide insert, wherein the coat proteins are able to assemble to form a modified virus.
- Ahlquist, U.S. Pat. 5,173,410, discloses a modified Brome Mosaic Virus in which the coat protein has been replaced with a CAT gene or fused to a CAT gene. Ahlquist does not disclose a modified virus comprising a coat protein

containing an foreign peptide insert, wherein the coat proteins are able to assemble to form a modified virus.

- Pelcher *et al.*, EP 067,553 (1982) disclose a potential method for making modified viruses containing a protein sequence fused to a coat protein. Pelcher *et al.* do not disclose a modified virus comprising a coat protein containing an foreign peptide insert, wherein the coat proteins are able to assemble to form a modified virus.
- Ahlquist *et al.*, "Sindbis Virus Proteins nsP1 and nsP2 Contain Homology to Nonstructural Proteins from Several RNA Plant Viruses" J. Virol. 53(2):536-42 (1985) describe sequence homologies between (+) stranded RNA viruses. Ahlquist *et al.* do not disclose a modified virus comprising a coat protein containing an foreign peptide insert, wherein the coat proteins are able to assemble to form a modified virus.
- Ahlquist *et al.*, "Nucleotide Sequence of the Brome Mosaic Virus and its Implications for Viral Replication" J. Mol. Biol. 172:369-83 (1984) describe the nucleotide sequence for Brome Mosaic Virus. Ahlquist *et al.* do not disclose a modified virus comprising a coat protein containing an foreign peptide insert, wherein the coat proteins are able to assemble to form a modified virus.
- Ahlquist *et al.*, "Complete Nucleotide Sequence of Brome Mosaic Virus RNA3" J. Mol. Biol. 153:23-38 (1981) describe the nucleotide sequence for Brome Mosaic Virus RNA3. Ahlquist *et al.* do not disclose a modified virus comprising a coat protein containing an foreign peptide insert, wherein the coat proteins are able to assemble to form a modified virus.
- Haselhof *et al.*, "Striking Similarities in Amino Acid Sequence Among Nonstructural Proteins Encoded by RNA Viruses that Have Similar Genomic Organization" Proc. Natl. Acad. Sci. USA 81:4358-62 (1984) described structural homologies between (+) stranded RNA viruses. Haselhof et al. do not disclose a modified virus comprising a coat protein containing an foreign peptide insert, wherein the coat proteins are able to assemble to form a modified virus.

This Information Disclosure Statement under 37 C.F.R. §§ 1.56 and 1.97 is not to be construed as a representation that a search has been made, that additional information material to the examination of this application does not exist, or that any one or more of these citations constitutes prior art.

Dated: August 19, 2002

David J. Wilson
Registration No. 45,225

MEDLEN & CARROLL, LLP
101 Howard Street, Suite 350
San Francisco, California 94105
617/252-3353